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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/031,087 | 02/26/1998 | CHIH-SHENG CHIANG | 054769-2001 | 8207 |

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| EXAMINER | |
|---|---|
| TUNG, JOYCE | |
| ART UNIT | PAPER NUMBER |
| 1637 | |

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| 07/16/2008 | PAPER |

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/031,087 | CHIANG ET AL. | |
| | Examiner | Art Unit | |
| | Joyce Tung | 1637 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *18 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *2-11 and 14-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2-11 and 14-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

The finality of the Office action mailed 3/22/07 is withdrawn in light of the new grounds of rejections. Claims 2-11 and 14-22 are pending.

### *Claim Rejections - 35 USC § 102*

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 2-7, 19-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Heller (5,565,322, issued Oct. 15, 1996) as evidenced by Mullis et al. (4,965,188, issued Oct. 23, 1990).

Regarding claims 2 and 19-21, Heller discloses a method for monitoring nucleic acid amplification comprising amplifying a target nucleic acid and monitoring said target nucleic acid during said amplification using a first oligonucleotide probe and a second oligonucleotide probe, said first probe (See column 21, lines 28-35, column 19, lines 24-56, fig.4, column 6, lines 38-52, column 28, lines 14-39);

i) hybridizes to said target nucleic acid;

ii) comprises a fluorophore (See column 28, lines 1-5); and

iii) not equal in length to said second probe (See column 28, lines 6-13);

said second probe;

i) hybridizes to said first probe; (See column 28, lines 8-11) and

ii) has a quencher molecule which quenches said first probe fluorophore when said first and second probes are hybridized to each other; and detecting fluorescence of said first probe fluorophore to monitor amplification, wherein an increase in fluorescence correlates with amplification (See fig.4, column 6, lines 38-52, and column 28, lines 14-39).

Regarding claim 3, Heller discloses that the fluorophore on the first probe and the quencher molecule on the second probe are on complementary base pairs (See column 28, limes 9-10).

Regarding claims 4-5, Heller discloses that the fluorophore and quencher molecules are within about 1-3 or more hybridized base pairs of each other (See column 13, lines 35-38).

Regarding claims 6, Heller discloses that the fluorophore is on the 5' terminal nucleotide of the first probe (See column 28, lines 1-5) and the quencher is on the 3' terminal nucleotide of the second probe (See column 28, lines 6-8).

Regarding claim 7, Heller discloses that the quencher is on the 5'terminal nucleotide of the second probe and the fluorophore is on the 3' terminal nucleotide of the first probe (See fig. 1a and 1b).

Regarding claim 22, Heller discloses that the longer probe binds preferentially to the target polynucleotide and when preferentially bound to the target polynucleotide the fluorescence intensity of the fluorophore is greater than the fluorescence intensity of the fluorophore when hybridized to the second probe (See column 28, lines 31-35).

Heller does not explicitly disclose that the amplification is carried out using a thermostable nucleic acid polymerase and a primer pair. However, as evidenced by Mullis et al. (4,965,188, issued Oct. 23, 1990), PCR amplification uses a thermostable polymerase (See column 7, lines 42-45) and a pair of primers (See the Abstract). Therefore by teaching PCR Heller inherently teaches thermostable polymerase and primers flanking target sequence.

***Claim Rejections - 35 USC § 103***

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 8-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heller (5,565,322, issued Oct. 15, 1996) as evidenced by Mullis et al. (4,965,188, issued Oct. 23, 1990).

Regarding claims 8-10, Heller does not explicitly disclose that the second probe is shorter than the first probe by deletion of 3 or more 3' terminal nucleotides from the nucleotide sequence

of the first probe. The second probe is shorter than the first probe by deletion of 3 or more 5' terminal nucleotides, and deletion of 1 or more 3' terminal nucleotides of the first probe.

However, Heller does disclose the length of the first probe and the second probe is not equal in which the quencher oligomer is 5 to 10 bases shorter (See column 28, lines 8-9).

One of ordinary skill in the art would have been motivated to optimize the length of the first probe and the second probe which is not equal by the steps as recited in the instant claims based upon the teachings of Heller because it was routine practice in the art to optimize a reaction condition. It would have been prima facie obvious to make the length of the first probe and the second probe which is not equal.

5. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Heller (5,565,322, issued Oct. 15, 1996) as evidenced by Mullis et al. (4,965,188, issued Oct. 23, 1990), as applied to claim 20 above, and further in view of Di Cesare (5,716784, issued Feb. 10, 1998).

The teachings of Heller are set forth in section 2 above. Heller does not disclose the limitations of claim 11.

Di Cesare discloses an improved assay to detect or measure target nucleic acid sequence replication in a thermal PCR amplification procedure (See column 2, lines 24-25). The analytical probe hybridized to the target nucleic acid is longer than the detection probe by 16 nucleotides at 3' terminal which hybridizes to the analytical probe and the Tms of the analytical probe and detection probe are 69.8 °C and 54.8 °C (see column 6, lines 8-16).

One of ordinary skill in the art would have been motivated to apply a first probe and a second probe which have a dissociation temperature difference of 2 degrees or more as taught by Di Cesare because by doing so, a homogeneous assay detection and/or measuring target nucleic

acid is improved (See column 2, lines 24-25). It would have been prima facie obvious to apply a first probe and a second probe which have a dissociation temperature difference of 2 degrees or more.

6. Claims 14-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Heller (5,565,322, issued Oct. 15, 1996) as evidenced by Mullis et al. (4,965,188, issued Oct. 23, 1990), as applied to claim 20 above, further in view of Hiroaki et al. (EP 0461 863 A1).

The teachings of Heller do not disclose that the target polynucleotide comprises hepatitis C virus genome, the probe has the sequence of SEQ ID NO: 3 and 4 and the primer has the sequence of SEQ ID NO: 1 and 2.

Hiroaki et al. disclose a highly sensitive detection system for NANB hepatitis virus at its gene level and oligonucleotide primer used for the system (See pg. 2, lines 31-32). The NANB hepatitis is termed hepatitis C virus (HCV) (See pg. 2, lines 10-12). A nucleotide sequence of the 5' noncoding region from HC-J1 has been identified (See pg. 3. lines 4-32). The primers used in the highly sensitive detection system for HCV corresponding to the part of the 5' noncoding region of HCV are disclosed (See pg. 3, lines 38-42). The nucleotide of the 5' noncoding region comprises SEQ ID NO: 1 and 3 and the complementary sequence of SEQ ID NO 2 and base pair 1-17 of SEQ ID NO: 4 (See pg. 7, lines 11-21 and pg. 8, lines 15-19).

One of ordinary skill in the art would have been motivated to apply these nucleic acid sequences disclosed by Hiroaki et al. as probes and primers for the specific detection of the target polynucleotide, hepatitis C virus because these nucleic acid sequences provide a highly sensitive detection system for NANB hepatitis virus at its gene level (See pg. 2, lines 31-32). It would have been prima facie obvious to apply SEQ ID NO: 1 and 2 as primers and SEQ ID NO: 3 and 4 as probes for the detection of the target polynucleotide, hepatitis C virus.

**Summary**

7. No claims are allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joyce Tung whose telephone number is (571) 272-0790. The examiner can normally be reached on Monday - Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Joyce Tung
July 11, 2008

/Teresa E Strzelecka/
Primary Examiner, Art Unit 1637
July 14, 2008